CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
PUBLIC REPORT 2007-3

Cyazofamid

Tracking ID Number 214117

DESCRIPTION OF ACTION

ISK Biosciences Corporation submitted an application for California registration of Ranman 400SC, EPA Reg. No. 71512-3. Ranman 400SC is a fungicide with limited systemic activity for control of oomycete fungi on tomatoes, potatoes, and cucurbit vegetables.

The Department of Pesticide Regulation (DPR) evaluated the product label and data and found them acceptable to support registration. Precautionary and first aid statements, personal protective equipment (PPE) requirements, and other protective measures on the product label adequately mitigate the potential health risks to applicators and handlers. DPR does not expect significant adverse environmental impacts to result from registration of Ranman 400SC.

The U.S. Environmental Protection Agency (U.S. EPA) registered Ranman 400SC conditionally on November 12, 2004. At that time, U.S. EPA identified labeling deficiencies and required ISK Biosciences Corporation to correct the deficiencies as a condition of registration. ISK Biosciences Corporation complied with the conditions of registration and Ranman 400SC was fully registered April 5, 2006.

BACKGROUND

Registrant:	ISK Biosciences Corporation
Common name:	Cyazofamid
Chemical name:	4-chloro-2-cyano-*N*,*N*-dimethyl-5-p-tolylimidazole-1-sulfonamid
Brand name:	Ranman 400SC
Uses:	Fungicide for use on tomatoes, potatoes, and cucurbit vegetables
Pests controlled:	Oomycete fungi
Type of registration:	Full Registration

Ranman 400SC fungicide is a liquid suspension containing 34.5% cyazofamid. The product is a limited systemic chemical that inhibits all stages of fungal development. It is used as a protectant fungicide applied before the crop is infected by disease, with good protection against disease expected over a 7 to 10 day period. The Ranman 400SC label recommends its use as part of an integrated pest management (IPM) program.

SCIENTIFIC REVIEW

A. Chemistry

1. Product Chemistry**:** DPR evaluated the submitted chemistry studies for Ranman 400SC. The results are summarized in Tables 1 and 2.

Table 1. Physical and Chemical Properties of Technical Cyazofamid

Properties	Values
Physical state	White powder
Density (20^{o})	1.446 grams (g)/milliliter (ml) (Bulk)
pH (1% solution)	4.9 @ 25°C
Melting point	152.7°C
Partition coefficient (K_{ow})	1585 (Log_p = 3.29)
Water solubility	0.107 mg/L @ pH 7 (20°C)
Vapor pressure	$<1.33 \times 10^{-5}$ Pa @ 25, 30, 35°C
Storage stability	Stable for 3 years

2. Residues in Food and Animal Feed**:** ISK Biosciences Corporation submitted an adequate residue analytical method. However, DPR did not evaluate residue data in compliance with OPPTS 860.1500 guidelines (in accordance with California Notice 2004-7).

3. Environmental Fate**:** The cyazofamid environmental fate data included hydrolysis, soil photolysis, aerobic soil metabolism, anaerobic and aerobic aquatic metabolism, aged leaching, soil adsorption/desorption coefficient, and terrestrial field dissipation. DPR found the studies to be satisfactory.

   Comparison of the cyazofamid environmental fate data to the U.S. EPA and California EPA ground water leaching criteria indicate that cyazofamid has the potential to leach. However, cyazofamid has very low aqueous solubility and a short hydrolytic half-life. Consequently, cyazofamid is not persistent or mobile in the soil, and would not be expected to leach to ground water. The potential to leach is summarized in Table 2.

Table 2. Comparison of U.S. EPA and California EPA Ground Water Leaching Criteria with Environmental Fate Study Results for Cyazofamid

Parameter	**Potential to Leach Value** (U.S. EPA)	**Potential to Leach Value** (California EPA)	**Experimental Value**	**Criteria Exceeded**
Water Solubility	> 30 ppm	> 3 ppm	0.107 ppm	No
Soil Adsorption Coefficient (K_d)	< 5 ml/g		8.47 ml/g (Loamy sand) 13.49-87.0 (Sandy loam) 4.64 (Sand)	No No Yes
K_{oc}		<1,900 ml/g	1293 ml/g (Loamy sand) 2172-1150 (Sandy loam) 736 (Sand)	Yes
Hydrolytic half life	> 30 days	> 14 days	< 13 days	No
Aerobic soil metabolic half-life	> 21 days	> 610 days	15 days (Loamy sand) 6.4-8.7 (Sandy loam) 9.9 (Sand)	No
Anaerobic soil metabolic half-life	> 21 days	> 9 days	< 6 days	No
Field dissipation half-life	> 21 days		3 days (All test soils)	No

The product chemistry, residue chemistry, and environmental fate data support registration of Ranman 400SC.

B. Toxicology

ISK Biosciences Corporation submitted adequate toxicology studies to conduct complete toxicological evaluations of Ranman 400SC. DPR evaluated the submitted data to determine the potential for adverse health effects. The acute toxicity parameters for Ranman 400SC are summarized in Table 3.

Table 3. Acute Toxicity of Ranman 400SC *		
Type of Study	**Acute Toxicity Values**	**Acute Toxicity Category**
Acute oral	LD_{50} > 5000 mg/kg	IV
Acute dermal	LD_{50} > 2000 mg/kg	IV
Acute inhalation	LC_{50} >5.5 mg/l	IV
Primary eye irritation	N/A	IV
Primary dermal irritation	N/A	IV
Dermal sensitization	N/A	Not a Sensitizer
Signal word	N/A	CAUTION

*Acute Toxicity Values expressed as:
LD_{50} = Lethal dose that kills 50% of the test population
LC_{50} = Lethal environmental concentration that kills 50% of the test population
N/A = Not applicable

The Medical Toxicology Branch initially recommended against registration of Ranman 400SC because the rat reproduction study was not acceptable. In response, ISK Biosciences Corporation submitted the data necessary to upgrade the study to acceptable. DPR's evaluation of the acute toxicity studies indicates that the studies are adequate for a complete toxicological evaluation. The acute health risks to human from exposure to cyazofamid are minimal due to its low mammalian toxicity. The product label adequately identifies the potential acute toxicity hazards indicated by the data reviewed, and the first aid statements and PPE are adequate for the indicated acute toxicity hazards.

DPR found the submitted toxicology studies for Ranman 400SC sufficient to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121, et seq.). DPR prioritizes pesticide active ingredients for risk assessment based on of the nature of the potential adverse health effects, the number of potential adverse effects, the number of species affected, no observable effect levels (NOELs), potential for human exposure, use patterns, and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being in moderate or low priority. At this time, cyazofamid has not been prioritized by DPR for risk assessment. A summary of Toxicology Data with additional cyazofamid toxicity information is available on the DPR public website at:: http://www.cdpr.ca.gov/docs/toxsums/pdfs/5930.pdf.

C. Health & Safety

DPR's evaluation of the medical management information on the Ranman 400SC label and the acute toxicity study results indicate that the product label bears all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product label bears an adequate First Aid statement. In addition, the product label requires applicators and other handlers to wear long sleeved shirt and long pants, chemical resistant gloves, and shoes plus socks. The instructions direct applicators/handlers to not allow contact of contaminated clothing with unprotected skin, and to wash personal protective equipment (PPE) separately from other laundry.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on mallard ducks, bobwhite quail, rainbow trout, honeybee, carp, bluegill sunfish, sheepshead minnow, *Daphnia magna*, eastern oysters, mysid shrimp, and Flathead minnow. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from an environmental exposure. Table 4 summarizes the results of these studies.

Table 4. Summary of Fish & Wildlife Toxicity Values*

Test Animal	Type of Study	Acute Toxicity Value**	Relative Toxicity
Mallard duck	Acute oral dose	>2000 mg/kg (LD_{50})	Relatively non-toxic
Bobwhite quail	Feeding (5 day)	>5000 mg/kg (LC_{50})	Relatively non-toxic
Mallard duck	Feeding (5 day)	>5000 mg/kg (LC_{50})	Relatively non-toxic
Mallard duck	Reproduction (20 weeks)	5000 ppm NOEC	N/A
Bobwhite quail	Reproduction (21 weeks)	5000 ppm NOEC	N/A
Rainbow trout	Accumulation and elimination water exposure (21 day)	BCF of 186 @1.0 μgl^{-1} BCF of 286 @10 μgl^{-1}	N/A
Bobwhite quail	Acute oral dose	>2000 mg/kg (LD_{50})	Relatively non-toxic
Honeybee	Acute contact	>100 µg a.i./bee (LD_{50})	Slightly toxic
Honeybee	Single acute oral dose	>151.7 µg a.i./bee (LD_{50})	Slightly toxic
Carp	Water exposure (96 hrs)	>1.4 mg a.i./l (LD_{50})	Moderately-toxic
Bluegill	Water exposure	>1.4 mg a.i./l (LD_{50})	Moderately-toxic

Table 4. Summary of Fish & Wildlife Toxicity Values*

	(96 hrs)		
Rainbow trout	Water exposure (96 hrs)	>1.4 mg a.i./l (LD_{50})	Moderately-toxic
Sheepshead minnow	Water exposure (96 hrs)	>167 µg a.i./l (LC_{50})	Highly-toxic
Dapnia magna	Water exposure (48 hrs)	>1.4 mg a.i./l (LC_{50})	Moderately-toxic
Eastern oyster	Water exposure (96 hrs)	14.7 µg a.i./l (EC_{50})	Extremely-toxic
Mysid shrimp	Water exposure (96 hrs) flow-through	87 µg a.i./l (LC_{50})	Extremely-toxic
Flathead Minnow	Early life stage (33 day)	90.1 µg a.i./l (NOEC) 179 µg a.i./l (LOEC) 127 µg a.i./l (MATC)	N/A

* The test substance used for the studies was the technical active ingredient.
** Acute toxicity values expressed as:
EC_{50} = Concentration of a toxicant causing a defined non-lethal effect in 50% of the test population
BCF = Bioconcentration factor
NOEC = No observed effect concentration
LOEC = Lowest observed effect concentration
MATC = Maximum Acceptable Toxicant Concentration

The data indicate that cyazofamid is relatively non-toxic to birds, slightly-toxic to honey bees, moderately-toxic to carp, rainbow trout, bluegill sunfish, and *Dapnia magna,* highly-toxic to sheepshead minnows, and extremely toxic to eastern oysters and mysid shrimp. To mitigate the hazards to aquatic organisms the Ranman 400SC label contains the Environmental Hazards warning, "Do not apply directly to water, to areas where surface water is present, or inter-tidal areas below the mean high water mark. Do not contaminate water when disposing of equipment washwater or rinsate."

E. Efficacy & Phytotoxicity

Cyazofamid is in the cyanoimidazole group of fungicides, which are used to control diseases caused by oomycete fungi. Ranman 400SC is labeled for control of late blight on tomatoes and potatoes and downy mildew and phytophthora blight on cucurbit vegetables. Cyazofamid inhibits fungal respiration and energy production in all stages of fungal development. Cyazofamid has limited systemic activity and is used as a protectant fungicide applied by ground or aerial spray.

Submitted efficacy and phytotoxicity studies indicate that Ranman 400SC provides effective control of oomycete fungi in tomatoes, potatoes, and cucurbit vegetables. Product labeling allows air and ground equipment application at a maximum of 16.5 fluid ounces per acre per season. Dilution rates for Ranman 400SC range from 5 gallons of water per acre for aerial applications to 100 gallons per acre for dilute ground applications. For applications using less than 60 gallons per acre, the label recommends that an organosilicone surfactant be added to improve spray coverage. Ranman 400SC is compatible with most other insecticides, fungicides, fertilizers and micronutrient products. The product label contains directions for jar testing to determine compatibility with other pesticides (fungicides, herbicides, insecticides, or miticides). Submitted product efficacy and phytotoxicity data are adequate to support registration of Ranman 400SC.

ALTERNATIVES

Ranman 400SC inhibits all stages of fungal development. It is used as a protectant fungicide to be applied before the crop is infected by disease, providing good protection against disease over a 7 to 10 day period. Ranman 400SC was first registered by U.S. EPA on November 12, 2004, and since that time no fungal resistance has been detected to date. The resistance risk is unknown but is assumed to be medium to high. Resistance management is required. Because fungal resistance has not been detected for Ranman 400SC, and it inhibits all stages of fungal development, it works well as part of an IPM program, which may include rotation with other fungicides, the use of disease resistant crop varieties, cultural practices, crop rotation, biological disease control agents, pest scouting, and disease forecasting systems aimed at preventing economic pest damage. A number of other active ingredients are registered for control of oomycete fungi. However, an effective IPM strategy requires the flexibility of a large number of comparable, but not exactly equivalent, pesticides in order to reduce the development of resistance.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of Ranman 400SC. The label and data were found acceptable to support registration. Cyazofamid is not persistent or mobile in the soil, and would not be expected to leach to ground water. Also, hazards to aquatic organisms are mitigated by the label Environmental Hazards warning. The acute health risks to human from exposure to cyazofamid are minimal due to its low mammalian toxicity. The precautionary and first aid statements on the product label, and the recommended protective measures mitigate potential health risks to persons who may be exposed to these pesticides. If a risk assessment conducted by DPR determines that exposure to cyazofamid may result in unacceptable margins of exposure, further restrictions will be placed on the use of cyazofamid at that time.